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COMMUNICATIONS

SOME NON-SURGICAL AIDS IN THE TREATMENT
OF GLAUCOMA

BY

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THE first statement that ought to be made on this subject is a confession of my belief that nearly all cases of glaucoma will sooner or later require surgical intervention. It has been my experience to see many more bad results from postponing this intervention than from unsuccessful operations. Many ophthalmologists, for some of whom I have great respect, seem to have a horror of operating in simple glaucoma, and it is hoped that these notes will not offer any encouragement to an opinion which has, I believe, often sacrificed a patient's only prospect for retaining useful vision. There are, however, certain cases in which operation is particularly inadvisable, or in which it is desired to postpone it for a certain time and in these cases we may be grateful for any additions to our non-surgical armamentarium. In the November *Arch. of Ophthal.* for 1928 I summarized experiences culled from the literature concerning a number of therapeutic measures which have recently come into use, especially in Germany, and the exact references mentioned here may be found in that article. A number of these seemed of doubtful value, or with not enough clinical evidence to justify their general use. I thought to-night I would select for a

more detailed discussion a few of the newer methods with which substantial results have been obtained, and especially those of which I have had experience.

It goes without saying that the miotics, eserine and pilocarpine, should be tried in most cases before anything else is done. In an untreated case of simple glaucoma, these miotics will nearly always produce some fall in tension, and will often keep the tension normal for varying periods of time. They should be used often enough to keep the tension normal, if possible, or to ascertain how low it can be kept by their means, and I do not see how this can be done except by giving the patient a solution to use at home, for instance a solution of eserine one grain to the ounce, to use three or four times a day. The constant use of eserine may produce conjunctival irritation and in a few cases a conjunctivitis resembling that caused by atropine and in these cases pilocarpine is to be preferred, or the alternate use of the two drugs. On account of the occasional occurrence of synechiae after prolonged miosis, pupils which remain very small should be allowed to return to normal size occasionally, or even be aided by a drop of homatropine or cocaine, the patient being watched carefully afterwards for a return of raised tension.

The great danger of miotics is that of overconfidence in their effect, so that the vision and especially the fields as well as the tension, should be watched carefully during their use. The observation of Thiel, now amply confirmed by others, should be remembered, namely, that there is a characteristic daily curve of intra-ocular tension in glaucoma patients, tension usually but not always being highest on arising in the morning and lowest at night; hence, it should be recorded in the morning when possible, and when the field is failing, even if our tonometric findings are normal, it must be considered that a rise of tension probably exists at some time of the day or night, or at least a tension too high for the lamina cribrosa of the particular patient. In these cases, and the more common ones where miotics exert their effect only for a time and then fail to have any effect, something else must be done. It is understood that a careful general examination of the patient has been made, and measures taken to reduce blood pressure and clear up obvious pathological changes which might be a factor in the case. Frankly, in my own experience no very brilliant results have been obtained in glaucoma by constitutional corrective measures and I have seen only two general conditions which seem to have an undoubted aetiological relationship to glaucoma. These are the so-called vaso-neurotic diathesis, and the related condition of bronchial asthma. The vaso-neurotic diathesis includes persons of unstable vaso-motor mechanism and usually of unstable nervous system, as shown by tachycardia, flushing, angio-neurotic oedema and urticaria. Müller's observations by capillary micros-

copy of such patients have been extended by Scheerer and Parrisius to glaucoma patients, a large number of whom showed changes characteristic of the vaso-neurotic diathesis.

I have seen a number of cases of glaucoma in which marked rises of tension could be observed to follow attacks of asthma, or emotional shock, and believe the great therapeutic agent against these factors, aside from adrenalin in true bronchial asthma, is mental and physical rest. In the case of many patients, as soon as it is found that under the best possible control of general factors, and with the use of miotics, high tension persists, operation had best be undertaken at once.

Further delay may be considered advisable under some of the following conditions :

In very advanced age or feeble health ; in secondary glaucoma where an access of inflammation is likely to follow any operation, especially in sympathetic ophthalmitis ; in patients who have lost the sight of one eye—especially after an operation, with the field cut down close to the fixation point in the remaining eye ; and lastly, in patients who refuse operation.

The cutting down of the field should not be ordinarily considered a contraindication to operation. While we know that following a successful filtering operation a loss of field may occur, which may involve the fixation-point, we also know that this same loss, followed by further loss, will occur in time if the tension remains high. When two precautions are observed, I believe these losses of field following operation may be made exceedingly rare. These are, to reduce the tension to as near normal as possible before operation so that the change in tension may not be too great, and to minimize the time during which the anterior chamber remains empty following operation, in which respect iridencleisis with running conjunctival suture presents advantages over trephining.

The best known of the newer methods of reducing tension is the use of adrenalin or glaukosan, which, although by no means original with Hamburger, has been popularised by his thirteen or more publications on the subject since 1923. Glaukosan is essentially nothing more than Hamburger's only too suggestive name for dextro-rotatory adrenalin, preferred to ordinary adrenalin because of the absence of systemic symptoms from rise of blood-pressure after its subconjunctival injection. While 1:1,000 solutions of adrenalin were ineffective by instillation, Hamburger found that a 2 per cent. solution of ordinary adrenalin when instilled several times during an hour, produced maximal mydriasis with a fall in tension as great as by subconjunctival injection of the 1:1,000 solution. He called this solution, to which was added an optically inactive substance produced in the manufacture of adrenalin, "linksglaukosan," or glaukosan. Because of its

strength, it is not to be used for injection, but for instillation only, the patient being placed in the supine position and two drops placed in the inner angle, after which the lids are held open for thirty seconds. This is repeated three to five times at fifteen minute intervals, according to the effect desired. I have made a two per cent. solution by dissolving one grain of adrenalin as provided in ampoules in 50 minims of distilled water, two drops of dilute hydrochloric acid being necessary to complete the solution. This gives similar results when used in the same manner as glaukosan but is not so stable. In most cases, the ordinary 1:1,000 adrenalin was used, first by subconjunctival injections of four to five minims, and later, by the method suggested by Gradle of inserting a cotton pledget soaked with the same amount under the upper lid and leaving it four minutes. Enough absorption occurs when it is used in this way so that the same effect on the pupil and tension occurs as by injection and without the systemic symptoms occasionally observed after injection. Only one or two instillations of two per cent. butyn are required as a preliminary, while with injections more thorough anaesthesia is required or pain will often be complained of. The effect of packs or injections on tension seems to be practically the same as that of glaukosan. Gredstedt, in a recent comparison of series where each was used, found the effect of adrenalin more marked and lasting. When the object is the dilatation of a contracted pupil in iritis, to break up adhesions, glaukosan or the two per cent. adrenalin solution present the advantage of being absorbed over the whole cornea and bulbar conjunctiva, so that a uniform dilatation is produced, with a better result in fresh synechiae than packs which affect most markedly the upper segment, or injections which affect the segment where the injection is made. I have only seen a few older synechiae which could be broken up by any of these methods, and have seen pupils dilate under them, only to return after twenty-four hours to their former size in spite of the subsequent use of atropine.

There is some difference of opinion among observers as to the type of case in which adrenalin is indicated. Most agree that it is ineffective in acute, absolute and haemorrhagic glaucoma. In secondary glaucoma and in iritis glaucomatosa, where it was enthusiastically recommended and where it would theoretically be of so much advantage by simultaneously dilating the pupil and lowering tension, a number of discouraging results have been reported. Vannas saw a rise of tension in three such cases and no effect in two others, and concludes that it is contraindicated in the presence of any inflammation. This agrees with my own experience, as I have seen two severe reactions in such cases with acute rise of tension. One was in a blind eye with a tension of sixty, containing a piece of copper, in which the patient wished to delay enucleation

several days. The pain following an adrenalin injection was so severe that he was glad to part with the eye the following day. The other case was a luetic patient with a haemorrhagic glaucoma in whom rise of tension with severe pain followed an adrenalin pack, lasting twenty-four hours, but resulting in a reduction of tension from forty to twenty-seven. These experiences have led me to discard the method in such cases, and reserve it for simple glaucoma, where it will serve, in a large percentage of cases, to reduce tension before operation, or when used with miotics, to allow postponement of operation for long periods.

Out of about one hundred treatments, the records of fifty are complete enough to be of any value. In two-thirds of these, packs were used, in the rest, subconjunctival injections. In fifteen cases, the treatment failed to produce an appreciable decrease of tension. These failures were in cases of iritis glaucomatosa 2, inflammatory glaucoma 2, absolute 1, secondary 1, acute 1, and simple 9 cases. In all the others, most being cases of simple glaucoma, a marked fall of tension occurred, the average decrease being 10 mm., while individual falls of 20, 23, and 24 mm. were recorded. In all but three of these, tension reached normal or below 25 mm. Schiötz. The tension was not taken often enough to determine the average duration of decreased tension, but in thirteen it remained normal one week or more and in five one month or more. Miotics had been tried in all cases before the treatment and were continued afterwards. Some cases left observation after one or more packs with tension still normal, while in a number of others later injections were less effective and operation was performed. Four cases have been followed for eight to twelve months, all having lost the sight of one eye elsewhere on other forms of treatment, and in these four vision has remained the same as at first, and tension has remained normal on miotics with an occasional pack, except in one case in which only a week ago the pack was finally ineffective and iridencleisis was performed on the only seeing eye. Certain cases responded much better to this treatment than others, and I have a distinct impression that it is especially apt to be effective in those of the vaso-neurotic type, who are subjects of vagotonia and hence would theoretically be especially responsive to the sympathetic stimulant adrenalin. I mention this with hesitation, as I know of no subject on which such floods of ink have been spilled to so little purpose as this one of vagotonia.

In simple glaucoma, the only complication seen was an acute rise of tension occurring in two cases which were reported in the *Amer. Jl. of Ophthal.* (1928, 11, p. 628). While no permanent ill effects resulted in these cases, they were especially dramatic as involving in each case the only seeing eye. In one, the tension remained high following paracentesis, but subsided during twelve

hours, then remained normal for two weeks under eserine, when it rose to 44 mm. (Schiötz) and iridencleisis was performed. In the other, it subsided after three hours and has remained about 14 mm. (Schiötz) for eight months up to the present time. These attacks, while rare, have been reported by others in simple glaucoma, and in one case, that of Böhm (*Arch. of Ophthal.*, 1928, p. 574), resulted in permanent reduction of vision to hand movements in one eye. In this case no miotics were used for two days afterwards and operation was delayed five days, and the disastrous result could probably have been prevented by miotics or paracentesis. It is on account of these occasional attacks, however, that I consider inadvisable the practice of Thiel, who gives patients an adrenalin ointment to use at home. These cases should be watched for some time after treatment. Eserine should be given twice at five minute intervals before treatment, and repeated once every twenty minutes in the first hour afterwards, and every half-hour in the next two hours, or often enough to keep the pupil small. This use of miotics does not lessen the effect of the drug on tension.

Before leaving the subject of adrenalin and glaukosan, aminoglaukosan must be mentioned, if only to clear up the confusion due to its name. This is Hamburger's name for a ten per cent. solution of histamin, a protein split product derived from ergot. It has the opposite effect of glaukosan, one drop instilled in the sac being sufficient to contract a pupil dilated by atropine to pin-point size in seven to fifteen minutes, according to Hamburger. It is recommended by him in acute glaucoma, the resulting miosis having reduced tension in a limited number of cases. Others, however, have reported failures and the accompanying chemosis of the conjunctiva has necessitated delaying a needed operation in several cases. I have seen such a severe inflammation follow its use in one case that I have not been encouraged to try it further.

Another procedure which will reduce tension in acute glaucoma, if only temporarily, and which has the virtue of being without danger, is the systemic use of hypertonic solutions. This is done with the idea of making the blood plasma hypertonic, causing absorption of fluids from all the tissues, including the eye, into the blood stream. That this actually occurs is attested by the results of Cantonnet, Hertel, Weekers and others. 35 to 50 c.c. of 30 per cent. or 100 to 150 c.c. of 10 per cent. sodium chloride are injected intravenously, the stronger solution producing the more rapid effect. Duke-Elder reports reduction of tension from 95 to 38 mm. by this method in one case and from 58 to 20 in another. He summarizes the indications for the method as follows:

"1. In acute glaucoma, in conjunction with miotics, before operation.

" 2. To reduce high tension before any operation. Besides lessening the danger of vitreous loss and haemorrhage, reduction of tension allows the absorption of local anaesthetics, which are ineffective in eyes with high tension.

" 3. In iritis glaucomatosa, before using atropine.

" 4. To facilitate ophthalmoscopic examination where the cornea is steamy from increased tension.

" 5. Is of possible value in any intraocular inflammation by withdrawing fluids from the eye, these being replaced by fresh fluids from the blood stream, bearing increased anti-bodies or drugs which have been given. It would act theoretically like a paracentesis."

As no traumatism is inflicted on the eye itself there is no danger in using this method in any form of glaucoma, and it does not increase the technical difficulties of operation, as amino-glaukosan may do.

Solutions of 30 per cent. glucose have been given by Sansum to produce the same effect on the blood, but large amounts must be given (300 to 500 c.c.). Magnesium sulphate in large doses by the mouth may also extract enough water from the blood by way of the intestinal tract to lower the intraocular tension and is used by neurological surgeons for the same effect on intracranial tension. The effect of these solutions by the mouth, while less rapid than when the intravenous route is used, is more prolonged.

I have had personal experience with this method (*i.e.*, the use of hypertonic solutions) in only three cases, having been deterred from using it by the time required for preparation of solutions and apparatus, and by the circumstances under which operations for acute glaucoma must often be done, but I believe the complications from operation, especially haemorrhage, would be less frequent if it were more often used, and that a few eyes might be brought under the influence of miotics so as to render operation unnecessary.

Of a number of drugs less well known in America than adrenalin, I have wished to discuss here gynergen or ergotamine, because the reports concerning it, while not as yet very numerous, seem to agree fairly well on the results of its use, and because I have had some experience with it. This is a derivative of ergot, containing the active principle used in obstetrics. It is used subcutaneously in a dosage of 1/250 grain or by mouth 1/60 to 1/30 grain. Besides causing contraction of the uterus, it raises the blood pressure. It depresses the sympathetic nerve-endings and its use in glaucoma is based on the idea that hypertension is due to hyperactivity of the sympathetic system, and that such a drug would decrease the permeability of the vessels.

Thiel reports on 90 cases of glaucoma in which ergotamine was used by subcutaneous injection of 1/4 mg. or by oral administration of one to three tablets of one mg., doses by each method being repeated three times a day. Rest for one hour after treatment is advised to avoid systemic symptoms observed in a few cases. A summary of results in these 90 cases is not given but a few illustrative cases show that in simple glaucoma the tension could be kept normal by oral administration of ergotamine for several months, and that after the first three to four weeks miotics which had been ineffective, were so much more effective that the ergotamine could be discontinued. In one of these cases the tension sank from 70 to 24 mm. after one subcutaneous injection. In iritis glaucomatosa and some cases of secondary glaucoma where iritis was present, good results were obtained, and in one of these an acute attack of glaucoma was aborted by one injection. No effect was secured in absolute glaucoma. In inflammatory glaucoma a fall from 72 to 24 was observed in one case. Römer and Krebs observed reductions of tension in glaucoma produced by ergotamine, but not so great as would be produced by adrenalin. Heim confirmed Thiel's observations in a series of cases and also found that after using fairly large doses for a variable time much smaller amounts were effective in keeping the tension normal, when combined with the use of miotics. The advantages of any method of treatment that can be given systematically, without traumatism to the eye, are obvious in certain cases of glaucoma.

I have used ergotamine in eleven cases of glaucoma in which operation was for some reason contraindicated. Five were cases of glaucoma after cataract operation, one of which was a traumatic cataract with anterior synechiae. Three were of glaucoma in sympathetic ophthalmitis, two were of simple glaucoma and one of absolute glaucoma. In most cases one-half c.c. of the solution was injected subcutaneously twice a day, in a few it was given by the mouth, from one to three pills three times a day. In two of the cases of glaucoma following cataract operation, the results were disappointing, tension being reduced only by 2 to 4 mm. (Schiötz) so that other means had to be employed. This was also true of the case of traumatic cataract. In one case, however, tension fell from 30 to 18 three hours after one injection and was kept down to 24 by oral administration, with an occasional injection, for three months, being 24 at the last examination, when vision with correction was 20/40 and no ergotamine had been used for several weeks. In another case tension fell from 32 to 24 and later from 37 to 17 mm. following injection, but these could not be continued on account of nausea.

In one case of simple glaucoma, where eserine and adrenalin packs had finally lost their effect, not enough effect was produced

by ergotamine to avoid operation. In the other case a fall of tension from 37 to 11 mm. occurred five hours after one injection but this was an atypical case whose tension varied greatly owing to other factors. In the case of absolute glaucoma, tension fell from 70 to 60 mm. following one injection and six oral doses. In one case of sympathetic ophthalmitis with iris bombé in a child of six, four oral doses caused a fall of tension from 44 to 37 in twenty-four hours, after which the case was not seen. In a second case which could be watched in the hospital, a regular effect of the drug was seen time after time, decreases of tension from 40 to 25 mm., and 35 to 20 mm. being recorded repeatedly. A slighter effect on tension was produced when the drug was given by mouth. In this case the use of gynergen was of the greatest value, as operation could be postponed for three weeks until much more favourable conditions were present and a post-operative rise of tension was controlled. In a third case tension was reduced from 32 to 19 mm. after one injection but three days later was 37 mm. and this time the drug was ineffective.

It will be seen that, as with adrenalin, cases vary greatly in their reaction to this drug, and that in a large proportion, its effect was not sufficient to avoid operation. This might be expected in the cases following cataract, where purely mechanical factors of drainage are apparently concerned, and still it was in one of these that the most brilliant result was obtained. If it were only for this case and the two cases of sympathetic ophthalmitis, I would feel that the time spent in experimenting with ergotamine was not wasted. I am sorry not to be able to report more experiences in simple glaucoma, which is where one would hope for the best results. One thing can be said for the drug, that it has caused no ill effects in my experience. One patient complained of such headache and discomfort following its use that it had to be discontinued, and one had diarrhoea, but the others noticed no subjective symptoms. The purpose of these notes is to show that it will decrease tension in certain cases, and that a trial of its effects is never harmful, unless too much time is wasted before a decision is arrived at.

The same may be said of several other drugs, pituitrin, tyramine and barium, from the reports of others, but since these reports were not so convincing as those concerning ergotamine, I have thought it best not to discuss them here. Brief notes concerning them will be found in the November *Arch. of Ophthal.*, 1928. With another method of treatment, the administration of calcium as calcium chloride internally, or as afenil intravenously, I have had no experience but believe that the method is worth mentioning. It rests upon the fact that calcium decreases the permeability of the capillaries, and the results of Weekers, Gowland, Alt, Kleiber and

von Hofe indicate a definite value in the method, which can be used with miotics. von Hofe found that calcium increased markedly the effect of adrenalin given subconjunctivally.

Summary

1. Adrenalin or glaukosan is of value especially in simple glaucoma, and by its means tension may be kept normal for considerable periods in certain cases.

2. Miotics should be used to prevent acute rise of tension when using adrenalin and to prolong its effect afterwards.

3. Amino-glaukosan presents the danger of increasing inflammation, and fails to reduce tension in many cases.

4. Hypertonic solutions can be depended upon to reduce tension before operation in acute glaucoma, and are without danger to the eye.

5. Ergotamine will reduce tension appreciably, it may be of much value in a small percentage of cases, and may be tried safely in any case.

6. All methods of treatment demand careful watch of the vision, fields and tension, so that progress of the disease may be noted early enough for effective surgical intervention.

A CASE OF MONOCULAR BLINDNESS OF ELECTRICAL ORIGIN*

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To my knowledge medical literature relates the observation of seven cases where the two eyes have been lost by the dazzling effect of electric light, after having been exposed to the intense luminous rays caused by lightning, by reverberation of the sun, and finally by a short circuit. As the patient—the subject of this work—has become blind of one eye only, after having been submitted, at a short distance, to the effects of electricity and of melting metal, I believe it interesting to publish his history, and will profit by this circumstance to recall the most recent theories on the injurious action of intense light in relation to the visual organ.

Case report.—On May 25, 1927, Mr. A. B., aged 37 years, labourer in a foundry, received the order to carry a bar of steel into an electrical soldering room. Entering these premises for

* Read before the 10th Congrès des Médecins de langue française de l'Amérique du Nord, Quebec, September, 1928.